

IN THE SPECIFICATION

The paragraph beginning on page 2, line 4 has been amended as follows:

Reactive oxygen species in general, and the molecule nitric oxide (NO) in particular, are key entities in the processes of atherosclerosis and restenosis. In endothelial cells, NO is formed from the metabolism of L-arginine by endothelial NO synthase (Oeamar *et al.*, "Reduced Endothelial Nitric Oxide Synthase Expression and Prosuction in Human Atherosclerosis." *Circulation* 1998, v. 97, 2494-2498). Under normal hemodynamic conditions, the production of NO inhibits such processes as monocyte adherence and chemotaxis, platelet adherence and aggregation, and vascular smooth muscle proliferation, all of which are potential causes of atherosclerosis and restenosis. In contrast, reduced NO expression has been associated with increased endothelial adhesiveness for monocytes and increased lesion formation in pathological rabbit models (Niebauer *et al.*, "Local L-Arginine Delivery After Balloon Angioplasty Reduces Monocyte Binding and Induces Apoptosis." *Circulation* 1999, v. 100, 1830-1835). Accordingly, NO is as a key entity in the balance of metabolic and biological processes involved in atherogenesis and restenosis.

The paragraph beginning on page 2, line 17 has been amended as follows:

Because of the small concentrations of NO expected *in vivo*, a more complete understanding of sample biological environments can be obtained by making measurements of superoxide concentration in addition to or independent of NO measurements. Superoxide is a key molecular entity in determining the balance of NO released by the endothelium. Superoxide free radicals can be released by activated monocytes and can counteract NO, in effect

neutralizing the beneficial properties of NO (Hishikawa and Luscher, "Pulsatile Stretch Simulates Superoxide Production in Human Aortic Endothelial Cells:" *Circulation* 1997, v. 96, 3610-3616). The ratio of NO concentration to superoxide concentration can therefore be a more useful measure than either concentration alone.

Q2 The paragraph beginning on page 3, line 18 has been amended as follows:

Other NO sensors employ methods including mass spectrometry, use of high-pressure cadmium columns (by measuring NO by-products), dithionite and hemoglobin treatment, solution methods, and electrical resistance across an electrode having a catalytic material capable of catalyzing oxidation of NO coated with a cationic exchanger. Superoxide detection methods are similar.

Q3 The paragraph beginning on page 5, line 1 has been amended as follows:

In accordance with another aspect of the embodiments of the invention, a diagnostic method is provided comprising positioning an elongated wire assembly into a vessel, the wire assembly including a sensor for measuring the level of nitric oxide or superoxide; guiding the wire assembly to a designated region within the vessel; and measuring the level of nitric oxide or superoxide in the region of the vessel. The method can further comprise inserting a catheter over the wire assembly to treat the region of the vessel. In one embodiment, a stimulant can be delivered to increase the production of nitric oxide or superoxide. The elongated wire can be used for the treatment of thrombosis or restenosis.

Q4 The paragraph beginning on page 6, line 16 has been amended as follows:

Figure 1 shows one embodiment of a guidewire 10 adapted to perform a therapeutic or diagnostic treatment. The use of the guidewire 10 is not limited to the treatment and diagnosis of a patient's vascular system, but can also include use with the esophagus, stomach, colon, uterus, joints, brain, liver, kidneys, ureter, urethra, bladder, mouth, nostrils, lungs, ~~esophagus~~, muscles, saphenous vein grafts or internal mammary artery grafts (and other arterial grafts such as radial grafts), and any other bodily organ capable of receiving a guidewire. Depending on the type of application in which it is to be used, the guidewire 10 can be used in conjunction with a variety of intravascular or intraluminal diagnostic or treatment devices, including balloon dilatation catheters (e.g., for percutaneous transluminal coronary angioplasty (PTCA) procedures), intravascular or intraluminal stents, directional atherectomy devices, drug delivery devices, radiation treatment devices, and devices for placing or retrieving vaso-occlusive coils.

(The paragraph beginning on page 12, line 10 has been amended as follows:)

Drug delivery catheters or stents can be used to administer any number of active agents. The active agent can be for inhibiting the activity of vascular smooth muscle cells. More specifically, the active agent can be aimed at inhibiting abnormal or inappropriate migration and/or proliferation of smooth muscle cells for the inhibition of restenosis. The active agent can also include any substance capable of exerting a therapeutic or prophylactic effect in the practice of the present invention. For example, the agent can be for enhancing wound healing in a vascular site or improving the structural and elastic properties of the vascular site. Examples of agents include antiproliferative substances such as actinomycin D, or derivatives and analogs thereof (manufactured by Sigma-Aldrich 1001 West Saint Paul Avenue, Milwaukee, WI 53233; or COSMEGEN available from Merck). Synonyms of actinomycin D include dactinomycin,

actinomycin IV, actinomycin I₁, actinomycin X₁, and actinomycin C₁. The active agent can also fall under the genus of antineoplastic, anti-inflammatory, antiplatelet, anticoagulant, antifibrin, antithrombin, antimitotic, antibiotic, antiallergic and antioxidant substances. Examples of such antineoplastics and/or antimitotics include paclitaxel (e.g., TAXOL[®] by Bristol-Myers Squibb Co., Stamford, Conn.), docetaxel (e.g., Taxotere[®], from Aventis S.A., Frankfurt, Germany), methotrexate, azathioprine, vincristine, vinblastine, fluorouracil, doxorubicin hydrochloride (e.g. Adriamycin[®] from Pharmacia & Upjohn, Peapack N.J.), and mitomycin (e.g., Mutamycin[®] from Bristol-Myers Squibb Co., Stamford, Conn.). Examples of such antiplatelets, anticoagulants, ~~antifibrin~~antifibrins, and antithrombins include sodium heparin, low molecular weight heparins, heparinoids, hirudin, argatroban, forskolin, vapiprost, prostacyclin and prostacyclin analogues, dextran, D-phe-pro-arg-chloromethylketone (synthetic antithrombin), dipyridamole, glycoprotein IIb/IIIa platelet membrane receptor antagonist antibody, recombinant hirudin, and thrombin inhibitors such as Angiomax[®] (Biogen, Inc., Cambridge, Mass.). Examples of such cytostatic or antiproliferative agents include angiopeptin, angiotensin converting enzyme inhibitors such as captopril (e.g., Capoten[®] and Capozide[®] from Bristol-Myers Squibb Co., Stamford, Conn.), cilazapril or lisinopril (e.g., Prinivil[®] and Prinzide[®] from Merck & Co., Inc., Whitehouse Station, NJ); calcium channel blockers (such as nifedipine), colchicine, fibroblast growth factor (FGF) antagonists, fish oil (omega 3-fatty acid), histamine antagonists, lovastatin (an inhibitor of HMG-CoA reductase, a cholesterol lowering drug, brand name Mevacor[®] from Merck & Co., Inc., Whitehouse Station, NJ), monoclonal antibodies (such as those specific for Platelet-Derived Growth Factor (PDGF) receptors), nitroprusside, phosphodiesterase inhibitors, prostaglandin inhibitors, suramin, serotonin blockers, steroids, thioprotease inhibitors, triazolopyrimidine (a PDGF antagonist), and nitric oxide. An example of an antiallergic agent is permirolast

Ab potassium. Other therapeutic substances or agents which can be appropriate include alpha-interferon, genetically engineered epithelial cells, rapamycin and dexamethasone.

The paragraph beginning on page 26, line 3 has been amended as follows:

The above embodiments can be used for superoxide sensors with minor modifications.

AG Superoxide sensors generally use different chemoluminescent and electrically reactive chemicals than NO sensors. Reactive chemoluminescent and electrically reactive methods for superoxide fiber optic sensors include nitro blue tetrazolium (NO₂-TB) method, cytochrome c method, epinephrine method, pyrogallol method and 6-hydroxydopamine method (Heikkilä, *et al.*, *Anal. Biochem.* 75: 356-362, 1972), and H₂O₂ measurement method, all of which are commonly used in the art.
